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Phototransformation of Napropamide [*N*,*N*-Diethyl-2-(1-naphthyloxy)propionamide] in Aqueous Solution: Influence on the Toxicity of Solutions

J. P. Aguer,[1]* P. Boule,[1] F. Bonnemoy[2] & J. M. Chezal[3]

[1] Laboratoire de Photochimie Moléculaire et Macromoléculaire, Université Blaise Pascal-CNRS, UMR 6505, F-63177 Aubière Cedex France
[2] UPRES-A 6023, Biologie Comparée des Protistes, F-63177 Aubière Cedex France
[3] Laboratoire de Chimie Organique, Faculté de Pharmacie, 28, Place Henri Dunant, F-63001 Clermont-Ferrand Cedex France

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Abstract: The main photoproducts formed in an aqueous solution of napropamide irradiated in UV light are *N*,*N*-diethyl-2-(1-hydroxynaphthalen-2-yl)propionamide, *N*,*N*-diethyl-2-(4-hydroxynaphthalen-1-yl)propionamide and 1-naphthol. These account for *c*.60%, 15% and 10% of napropamide converted respectively. No influence of the irradiation wavelength or of oxygen was observed. The same products were obtained by irradiation of methanolic solutions. The three identified products result from the cleavage of naphthoxy–carbon bond. The first two products imply a photo-Fries rearrangement. The influence of irradiation on the toxicity of the solutions was studied by the Microtox® test. The significant increase observed may be attributed partly to the formation of 1-naphthol. © 1998 Society of Chemical Industry

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Key words: napropamide; photolysis; aqueous solution; toxicity

1 INTRODUCTION

Napropamide [*N*,*N*-diethyl-2-(1-naphthyloxy)propionamide] (Fig. 1) is a selective systemic herbicide used for the pre-emergence control of annual grasses and broad-leaved weeds in various crops.[1] It inhibits root development and growth. Its acute oral LD_{50} for rats is higher than 5 g kg^{-1}. It is a moderate eye irritant but not a skin irritant for rabbits.

As a consequence of its utilisation, napropamide may be found in the soil and in the aquatic system. The fate of napropamide in the environment has been the theme of several publications.[2–5] In soil, degradation by micro-organisms is slow, transformation into naph-

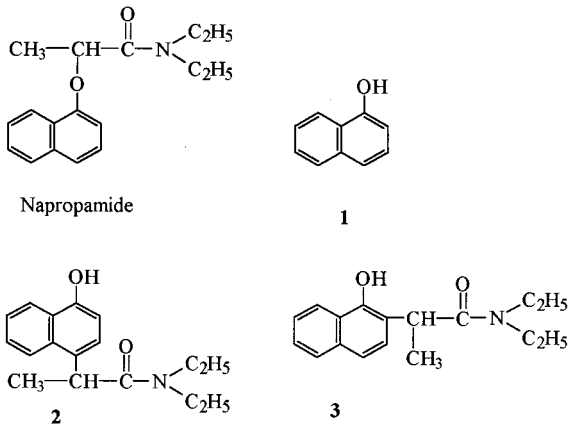

Fig. 1. Structures of compounds studied.

* To whom correspondence should be addressed.

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thoxypropionic acid being almost quantitative.[1] Photodegradation is expected to play a significant role since it absorbs sunlight in the range 290–350 nm, but data concerning its phototransformation are a little confusing. Stanger and Vargas,[3] and Donaldson and Miller[4] studied the kinetics of photodegradation in soils but the photoproducts were not analysed. The Pesticide Manual[1] reports that 'photodegradation is an important mechanism for loss from soil. 2-(α-naphthoxy)-*N*-ethylpropionamide, 2-(α-naphthoxy)propionamide, 1-naphthol and 1,4-naphthoquinone have been identified as degradation products,' but no reference to the original work is given. In a detailed study, Chang *et al.*[5] reported that the major photodegradation products were *N*,*N*-diethyl-4-hydroxy-α-methyl-1-naphthaleneacetamide and *N*,*N*-diethyl-1-hydroxy-α-methyl-2-naphthaleneacetamide.[5] These products result from a photo-Fries rearrangement. Such a reaction was recently observed with 1- and 2-naphthyl acetates.[6] Other products resulted from the coupling of the second primary photoproduct,[5] but no formation of naphthol was observed.

The photodegradation of napropamide may be compared to that of 2-naphthoxyacetic acid, which is transformed into 2-naphthol together with minor amounts of 2-hydroxy-1-naphthaldehyde and naphtho[2,1-*b*]furan-2 (1*H*)-one.[7]

In this context, the photochemical behaviour of napropamide in aqueous solution was studied under various conditions of wavelengths and in methanol, with a double goal: to clarify the stoichiometry of the reaction and to examine, using the Microtox® method, the influence of irradiation on the toxicity of the solutions.

2 MATERIALS AND METHODS

2.1 Reactants

Napropamide (99%) was provided by Chem Service. The other reactants were of the highest grade available and used as received. Water was purified with a Millipore Milli-Q-device. Methanol was a Carlo Erba product (HPLC grade, purity 99·9%). Solutions were deoxygenated by bubbling with nitrogen.

2.2 Irradiations

Aqueous solutions were irradiated at 253·7 nm in a cylindrical quartz cell located on the axis of a cylindrical mirror equipped with six monochromatic low-pressure mercury lamps (germicide lamp, Philips TUV 15 W). A similar device equipped with fluorescent lamps (Duke Sunlamp GL20) emitting between 275 and 350 nm with a maximum emission at 310 nm was also used to irradiate methanolic and aqueous solutions. The irradiation range was limited at 290–350 nm using a reactor screened with Pyrex. The quantum yields at 313 nm were determined by using a Bausch and Lomb monochromator equipped with a high-pressure mercury lamp. The beam was parallel and the reactor was a square quartz cuvette with a 1-cm path length. The incident light intensity at this wavelength was evaluated at $1{\cdot}3 \times 10^{15}$ photon s^{-1} cm^{-2} by ferrioxalate actinometry. Some aqueous solutions were irradiated at 365 nm in a water-cooled reactor using three 'black light' lamps (HPW 125 W Philips); about 85% of the energy was emitted at 365 nm and 7% at 334 nm.

2.3 Analyses

Absorption spectra were recorded on a Cary 13C Varian spectrophotometer.

HPLC analyses were performed on a Merck chromatograph with a photodiode array detector. The column was a Hewlett Packard reverse-phase C_{18}, 5 μm (250 × 4 mm), with methanol + water (66 + 34 by volume) as the eluent. Preparative HPLC was carried out on a Gilson chromatograph with a Microsorb C_{18} column, 3 μm (250 × 20 mm).

Mass spectra were obtained on an HP 5989 B in Laboratoire de Chimie Analytique, UFR de Pharmacie, Université d'Auvergne, France.

[^{1}H]NMR spectra were recorded on Bruker AC 400 MHz Fourier transformed spectrometer, using solutions in deuterated chloroform (Aldrich).

2.4 Evaluation of toxicity

The toxicity of irradiated solutions of napropamide was evaluated with the Microtox® technique (Microbics Corp. 1992) and compared with the toxicity of 1-naphthol. This method is based on the bioluminescence of the marine bacterium *Photobacterium phosphoreum* Ford, which can be inhibited by a toxic substance when the electron flux of the respiratory chain and consequently the metabolic activity of the bacterium is disturbed. The Microtox® technique is used to evaluate the concentration which inhibits 50% of the bioluminescence (CE_{50}). This rapid and reproducible test is becoming a reference test in ecotoxicology.[8,9]

3 RESULTS

The solubility of napropamide in water was determined as 73 mg $litre^{-1}$.[1] Aqueous solutions were stable in the dark: no change was observed in the UV-visible spectrum after 24 h at room temperature.

The first maximum in the UV absorption band is located at 288 nm. At this wavelength the molar

absorption coefficient has been evaluated at 5800 M^{-1} cm^{-1} (Fig. 2). The absorption is negligible at $\lambda > 350$ nm.

The following values were obtained for napropamide in $CDCl_3$: [^{1}H]NMR (400 MHz) δ (ppm): 1·00 (t, CH_3, J = 7 Hz), 1·15 (t, CH_3, J = 7 Hz), 1·75 (d, CH_3, J = 6·7 Hz), 3·40 (m, CH_2), 3·55 (m, CH_2), 5·15 (q, CH, J = 6·7 Hz), 6·85 (d, H_2, J = 8·2 Hz), 7·35 (t, H_3, J = 8·2 Hz), 7·45 (d, H_4, J = 8·2 Hz), 7·50 (m, H_6, H_7), 7·80 (dd, H_5 or H_8, J = 6·9 and 2·5 Hz), 8·35 (dd, H_8 or H_5, J = 6·9 and 2·5 Hz).

3.1 Irradiation between 290 and 350 nm

When an air-saturated aqueous solution of napropamide (10^{-4} M) in pure water at natural pH (pH 5·9) was irradiated between 290 and 350 nm, the absorption increased in the range 240–270 nm and at wavelengths >300 nm. No new typical band was observed in the spectrum. Three photoproducts appeared in the HPLC chromatogram of the irradiated solution (Fig. 3). In the first stage of the reaction the concentration of these photoproducts was proportional to irradiation time, which is consistent with primary products. The same reaction was observed in a solution deoxygenated by nitrogen bubbling.

The quantum yield of disappearance was evaluated at 0·25 in aerated solution.

3.2 Identification of photoproducts

Photoproduct **1** was identified as 1-naphthol by comparison of the retention time and the UV spectrum with

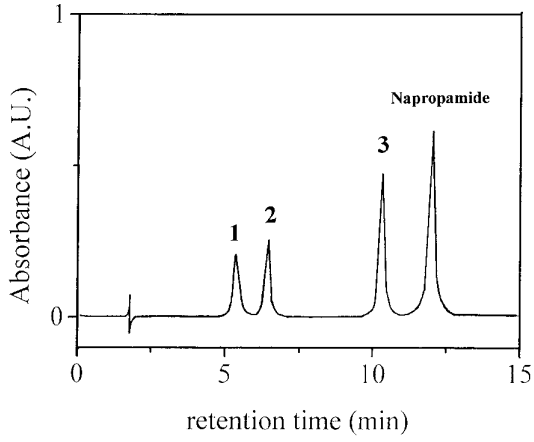

Fig. 3. HPLC chromatogram of an aqueous solution of napropamide (10^{-4} M) irradiated between 290 and 350 nm. Detection at 288 nm. Eluent: methanol + water (66 + 34 by volume).

those of a standard (Fig. 2). This assignment was further confirmed by the mass spectrum of the product isolated by preparative HPLC (main peak at $m/z = 144$).

The UV spectra of **2** and **3** are given in Fig. 2. Results of mass spectrometry and [^{1}H]NMR shifts in deuterochloroform are gathered below:

Product 2

m/z (relative abundance): 271 $[M]^{+\cdot}$ (14); main fragments: 171 (100), elimination of CO-NEt_2; 100 (68), CO-NEt_2; 72 (63), NEt_2.

[^{1}H]NMR (400 MHz) δ (ppm): 0·90 (t, CH_3, J = 7·1 Hz), 1·15 (t, CH_3, J = 7·1 Hz), 1·55 (d, CH_3, 6·8 Hz), 2·90 (m, CH_2), 3·10 (m, CH_2), 3·25 (m, CH_2), 3·60 (m, CH_2), 4·45 (q, CH, J = 6·8 Hz), 6·70 (s, OH), 6·80 (d, H_2, J = 7·9 Hz), 7·25 (d, H_3, J = 7·9 Hz), 7·50

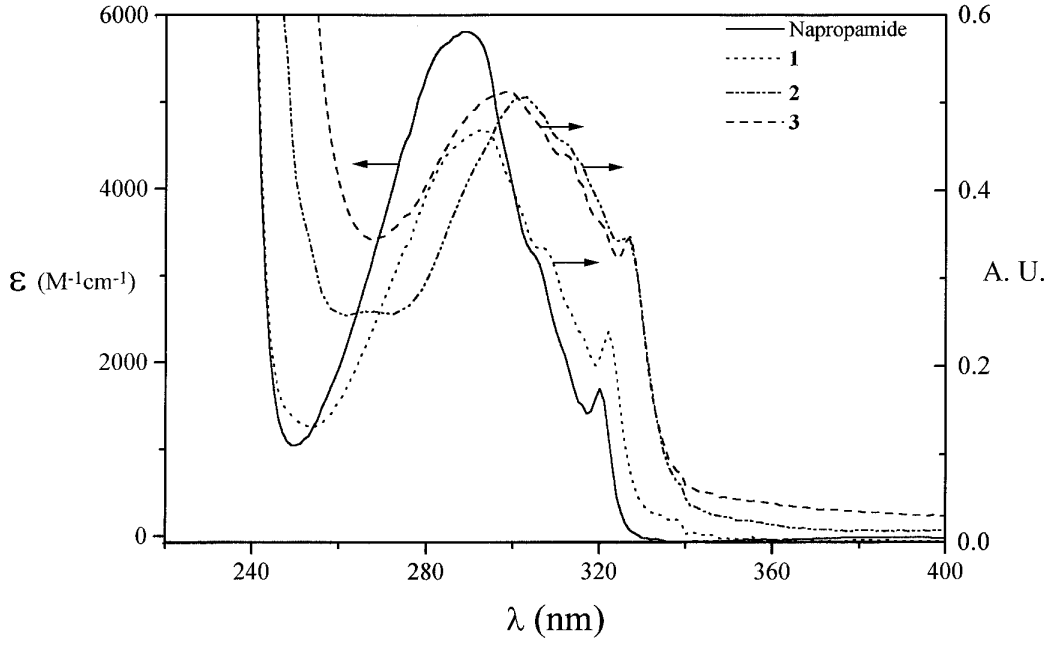

Fig. 2. UV spectra of aqueous solutions of napropamide and photoproducts.

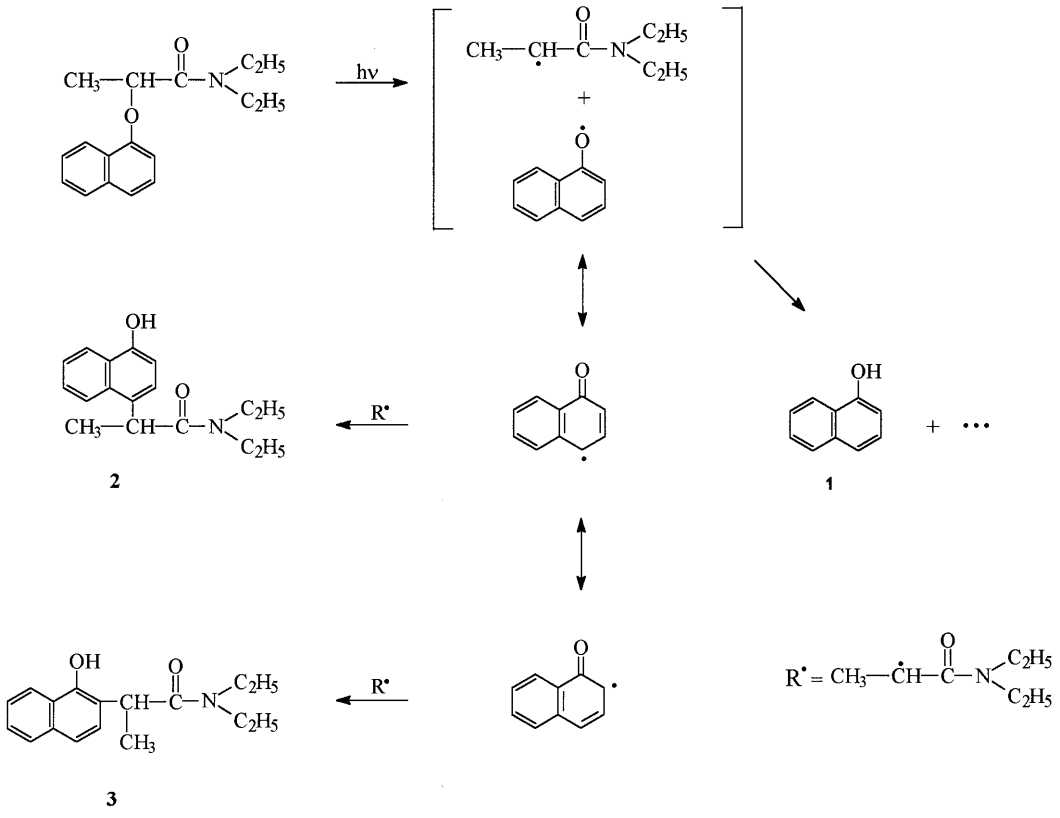

Fig. 4. Proposed reaction mechanisms.

(td, H_6 or H_7, J = 7·6 and 1·4 Hz), 7·60 (td, H_7 or H_6, J = 7·6 and 1·4 Hz), 8·00 (dd, H_5 or H_8, J = 7·6 and 1·4 Hz), 8·30 (dd, H_8 or H_5, J = 7·6 and 1·4 Hz).

Product 3

m/z (relative abundance): 271 $[M]^{+\cdot}$ (12); main fragments: 198 (35), elimination of NEt_2 ; 170 (100), elimination of $HCO\text{-}NEt_2$; 72 (41), NEt_2.

[^{1}H]NMR (400 MHz) δ (ppm): 1·15 (t, CH_3, J = 7·2 Hz), 1·35 (t, CH_3, J = 7·2 Hz), 1·55 (d, CH_3, 7·2 Hz), 3·50 (m, CH_2), 3·60 (m, CH_2), 4·05 (q, CH, J = 7·2 Hz), 7·10 (d, H_3, J = 8·3 Hz), 7·30 (d, H_4, J = 8·3 Hz), 7·45 (m, H_6, H_7), 7·74 (dd, H_5 or H_8, J = 7·5 and 1·6 Hz), 8·40 (dd, H_8 or H_5, J = 7·5 and 1·6 Hz), 11·60 (s, OH).

The [^{1}H]NMR spectrum of **3** in deuterium oxide is very similar except that the singlet at 11·6 ppm was not observed. This observation is in good agreement with the presence of a phenolic proton which is exchanged with deuterium in deuterium oxide.

From these results **2** and **3** were identified as *N,N*-diethyl - 2 - (4 - hydroxynaphthalen - 1 - yl)propionamide and *N,N*-diethyl-2-(1-hydroxynaphthalen-2-yl)propionamide, respectively. In order to evaluate the yields of conversion of napropamide into **1, 2** and **3**, these photoproducts were isolated by preparative HPLC. Solutions of known concentration were then prepared and used for the calibration of HPLC chromatograms. It was deduced that **3** is the main photoproduct and accounted for about 60% of napropamide transformed. The formation of **1** and **2** was estimated at 10 and 15% respectively.

TABLE 1

Effect of Napropamide and Photoproducts on Bioluminenscence of *Phosphobacterium phosphoreum* after 5, 15 and 30 min (Normalised Times of Contact used in the Microtox® Test)

	CE_{50} (*mg litre*$^{-1}$) (±*SD*)[a]		
	5 min	*15 min*	*30 min*
Napropamide	54·8 (7·0)	51·8 (6·2)	48·9[b]
1-Naphthol	2·61 (0·15)	2·84 (0·09)	2·84 (0·15)
Solution 30% transformed	21·3 (1·0)	23·9 (1·2)	25·5 (3·1)
Solution 90% transformed	12·3 (1·7)	14·5 (2·1)	16·4 (1·3)

[a] $n = 4$.

[b] Only one test.

3.3 Influence of irradiation wavelength

In order to study the influence of the irradiation wavelength, aqueous solutions were irradiated at 253·7 nm (reactor in quartz) or with 'black light' lamps (reactor in Pyrex). In both cases the same photoproducts **1, 2, 3** were obtained. With 'black light' the transformation

may be attributed to the minor line at 334 nm (about 7% of photons) since napropamide does not absorb at 365 nm.

An aqueous solution (10^{-4} M) was exposed to sunlight in summer in Clermont-Ferrand (latitude 46°N; 400 m above sea level) in a cylindrical Pyrex reactor (diameter 3 cm; length 30 cm). After 20 min the conversion was estimated at 50% and products **1, 2** and **3** were formed.

3.4 Irradiation of napropamide in methanolic solution

The irradiation of a solution (10^{-4} M) in the range 290–350 nm yielded products **1, 2** and **3**. It was noted that the formation of products was the same in air-saturated solution or after elimination of oxygen by nitrogen bubbling. In methanol the quantum yield was estimated at 0·20, i.e. not significantly different from the quantum yield in aqueous solution.

3.5 Mechanism

The three photoproducts result from the cleavage of the aryloxy–carbon bond. The propionamide moiety is eliminated or substitutes the aromatic ring in the *ortho* or *para* position. This substitution usually called photo-Fries rearrangement, can be explained by a radical mechanism (Fig. 4).

3.6 Influence of irradiation on the toxicity of solutions

Experiments were carried out with napropamide, 1-naphthol and solutions irradiated up to 30% and 90% conversion. In the case of irradiated solutions, it was assumed that the total number of molecules stayed the same. With the calculated values of CE_{50}, a comparison can be established between the toxicities of napropamide and its photoproducts. A decrease in CE_{50} involves the formation of products more toxic than napropamide. Results are collected in Table 1.

It can be seen that 1-naphthol is much more toxic than napropamide to *P. phosphoreum* and that irradiation of the solutions increases their toxicity. It has previously been reported that 1-naphthol is quite toxic.[10] The increased toxicity of the irradiated solutions is partly due to the formation of naphthol. It would be useful to have tested the toxicity of the other photoproducts; unfortunately the amount of isolated product was not sufficient to permit this. To evaluate the impact of photoproducts on the environment, it would be useful to complement the present test by other tests on daphnia, on protozoa and perhaps on other living organisms.

4 CONCLUSION

Our analytical results are in good agreement with those of Chang *et al.*,[5] with the difference that they did not observe the formation of naphthol and we did not detect the formation of the dimer, possibly because we used only UV detection for HPLC or because it is formed in the second stage of the reaction.

From the Microtox® test it appears that irradiation drastically increases the toxicity to *Phosphobacterium phosphoreum*, possibly because of the formation of naphthol.

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